UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/281,717	03/30/1999	JOHN D. BAXTER	9811-008-999	7561

7590 07/17/2002

PENNIE & EDMONDS LLP
1155 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-2711

EXAMINER
MORAN, MARJORIE A

ART UNIT	PAPER NUMBER
1631	23

DATE MAILED: 07/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/281,717	BAXTER ET AL.	
	Examiner	Art Unit	
	Marjorie Moran	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,30 and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 April 2002* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Continu d Examination Und r 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/25/02 has been entered.

Claims 1-16 and 30-31 are pending. All rejections and objections not reiterated below are hereby withdrawn.

Drawings

The drawings are objected to because Figure 7 incorrectly labels an NR-box, as admitted by applicant in the response filed 4/25/02. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Applicant is reminded that corrections to the drawings not supported by the originally filed specification, drawings, and/or claims may be considered new matter.

Claim Objections

Claims 3 and 12 are objected to because of the following informalities. Claim 3 recites Val184. No crystallographic coordinates for this position are disclosed by the specification, in Table1, or in the claims. As this is assumed to be a typographical error, (i.e. the claim should recite --Val284--, claim 3 is merely objected to herein. Applicant is advised that is this is not a typographical error, then claim 3 may be rejected for lack of written description and

lack of enablement. In claim 12, "a" before "in vivo" should be --an--. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 2-9 recite limitations with regard to homology to residues of a human thyroid receptor (TR) and identified residues by number (position) and amino acid. At least two different human thyroid receptors are known in the art and are designated alpha and beta (see e.g. instant Figure 19, NCI accession number P10828 (beta) and accession number CAA68539 (alpha). While similar, the alpha and beta forms of the thyroid receptor have different sequences and the amino acids are numbered differently. To elucidate: instant claim 2 recites residue Val284. Position 284 of TR-beta is a lysine, while position 284 of TR-alpha is an arginine. The specification teaches that the TR crystallized by applicants is the beta form, and Table 1 teaches residue numbers associated with particular amino acids, therefore the claims are enabled. However, given the fact that two TR's are known in the art, and the fact that the residues of TR-alpha are different than that for TR-beta, one skilled in the art would not know what TR and/or which residues must be used for the homology alignment, therefore the metes and bounds of applicant's invention are unclear and claims 2-9 are indefinite.

Claim Rejecti ns - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-10, 12-15, and 30-31 are rejected under 35 U.S.C. 102(e) as being anticipated by SCANLON et al. (US 6,26,622, filed Dec. 13, 1996).

SCANLON teaches a method of identifying a compound which selectively modifies the activity of a nuclear receptor (i.e. a coactivator), specifically a thyroid receptor, or of identifying an agonist or antagonist, by using the atomic coordinates of the receptor, specifically its ligand binding domain (LBD) to model compounds which fit spatially into the LBD using a computer, screening the test compounds in an in vivo or in vitro assay, then identifying the test compound which selectively modifies activity of the receptor or is an agonist or antagonist (col. 9, line 59-col. 10, line 36), thereby anticipating claims 1, 9-10, 12, and 30-31. SCANLON specifically teaches that his antagonists or agonists can block or promote binding of a coactivator (col. 24, lines 45-65), thereby anticipating claim 14. SCANLON teaches that his compounds may be peptides, peptidomimetics, or synthetic compounds (col. 3, lines 63-65), or may be from a

collection of compounds designed around a scaffold (i.e. a library; col. 32, lines 39-48), thereby anticipating claims 14-15. SCANLON specifically teaches fitting of compounds to TR-beta wherein the atomic structural model of TR-beta comprises coordinates for amino acids Ile280, Thr281, Val283, Val284, Ala287, Lys288, Phe293, Gln301, Ile302, Leu305, Lys306, Cys309, Pro453, Glu457, Val458, Phe459 (Appendices 7 and 8), thereby anticipating claims 2-8.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-15 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over SCANLAN *et al.* (US 6,266,622) in view of KUNTZ *et al.* (IDS document: Science 257, pp. 1078-1082. (1992)).

Claim 1 recites a method of identifying a compound which binds to a coactivator binding site of a nuclear receptor wherein test compounds are fit into the binding site using an atomic structural model of the receptor's coactivator binding site or portion thereof, screening the test compounds in a binding assay and identifying compounds that bind to the coactivator binding site. Claims 2-8 limit the atomic structural coordinates. Claim 9 limits the receptor. Claims 10 and 12 limit the binding assay to an in vitro or in vivo assay. Claim 11 limits the screening to high throughput screening. Claims13-15 limit the test compound. Claim 31 limits the method to one wherein the atomic coordinates are provided to a computerized modeling system. Claim 30 recites a compound identified by the method.

SCANLON teaches a method of identifying compounds which bind to a ligand binding site on a thyroid receptor and alter the activity of the receptor (e.g. a coactivator), as set forth above. SCANLON does not teach high throughput screening.

KUNTZ teaches use of high throughput screening in combination with computer screening/modeling to identify ligands for various proteins (pp. 1080-1081). KUNTZ specifically teaches that robotic systems make it feasible to scan entire databases of compounds (p. 1078).

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the high throughput, robotic screening of KUNTZ in the method of SCANLON where the motivation would have been to screen large numbers of compounds in a method to identify coactivators, as suggested by KUNTZ' teaching that lead discovery (e.g. of drug candidates) will proceed more rapidly by combining computer screening and high volume (throughput) assays (p. 1081). One skilled in the art would reasonably have expected success in combining the high throughput assays of KUNTZ with the method of SCANLON because both teach combining test assays with computer modeling/screening steps, and both teach that such assays can be used to identify compounds which bind to receptors.

Claims 1-10, 12-16, and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over SCANLAN *et al.* (US 6,266,622) in view of HEERY *et al.* (IDS document: Nature (1992), vol. 387, pp. 733-736).

The claims recite a method of identifying a compound which binds to a coactivator binding site of a nuclear receptor, as set forth above. Claim 16 limits the test compound to be a peptide comprising a nuclear receptor box.

SCANLON teaches a method of identifying compounds which bind to a ligand binding site on a thyroid receptor and alter the activity of the receptor (e.g. a coactivator), as set forth above. SCANLON does not specifically teach peptides comprising nuclear receptor boxes.

HEERY teaches motifs comprising an LxxLL sequence which are necessary and sufficient for binding of coactivators to ligand binding domains of nuclear receptors (p. 733, abstract). As HEERY teaches motif sequences which are identical to those exemplified by applicant as being "nuclear receptor boxes" (See instant Figure 7 and the TIF2 sequences taught by HEERY on p. 735, Figure 2a), the motifs taught by HEERY are interpreted to "nuclear receptor boxes".

It would have been obvious to one of ordinary skill in the art to have used peptides comprising the LxxLL motif taught by HEERY as the test compounds in the method of SCANLON where the motivation would have been to enhance success in identifying coactivators by screening peptides comprising a sequence/motif already known to be present in known coactivators of nuclear receptors, as suggested by the teaching of HEERY that an LxxLL motif is both necessary and sufficient for binding of coactivators to nuclear receptors (p. 734). One skilled in the art would reasonably have expected success in screening peptides comprising the LxxLL motif of HEERY in the method of SCANLON because SCANLON teaches that peptides may be screened in his method and HEERY teaches that peptides comprising his motif can be screened for binding/coactivator activity (p. 735, Figure 3).

Conclusion

Claims 1-16 and 30-31 are rejected. Claims 3 and 12 and the drawings are objected to.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to a patent analyst, Tina Plunkett, whose telephone number is (703) 305-3524.

Marjorie A. Moran
Examiner
Art Unit 1631

July 12, 2002